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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,583	01/09/2006	Michael Crager	INTM-016	7017

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Li-Hsien(Lily) Rin-Laures
Marshall, Gerstein & Borun LLP
233 South Wacker Drive
6300 Sears Tower
Chicago, IL 60606-6357

EXAMINER	
HISSONG, BRUCE D	
ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,583	CRAGER ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicant's submission of the specification, drawings, and claims of the instant application on 2/23/2005 has been entered into the record.

2. Claims 1-35 are currently pending and are the subject of this office action.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because it has not bee signed by each inventor. Applicants petition to allow inventor Crager to make an application on behalf of himself and on behalf of the joint inventor who has not joined in the application, submitted on 1/9/2006, is noted. However, this petition was dismissed for reasons noted in the petition decision mailed on 5/18/2006. In view of the dismissal of said petition, the oath and declaration is objected to as being defective.

Claim Objections

The Examiner suggests amending claim 1 to recite "an effective amount of interferon (IFN)-γ" in order to define the acronym IFN.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 and 27-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating an individual with idiopathic pulmonary fibrosis (IPF) wherein said "treating" comprises increasing survival time or decreasing the risk of death due to disease, does not reasonably provide enablement for a method of treating IPF wherein said "treating" comprises preventing the disease from occurring in a subject which may be predisposed to the disease but has not yet been diagnosed as having it, or inhibiting/arresting the disease, or relieving the disease/causing regression of the disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. Ex Parte Forman, (230 USPQ 546 (Bd. Pat. App. & Int. 1986); In re Wands, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The claims of the instant invention are drawn to a method of treating IPF in an individual, the said method comprising administering to the individual an effective amount of interferon (IFN)-γ. The specification, paragraph 0011 (p. 2), defines the terms "treatment", "treating", and the like, to refer to any treatment of a disease in a mammal, particularly a human, and includes (a) increasing survival time; (b) decreasing the risk of death due the disease; (c) preventing the disease from occurring in a subject which may be predisposed to the disease but has not yet been diagnosed as having it; (d) inhibiting the disease, i.e. arresting its development (e.g. reducing the rate of disease progression); and (e) relieving the disease, i.e. causing regression of the disease.

The specification provides guidance and examples showing that administration of IFN-γ to individuals suffering from IPF, wherein these individuals had a forced vital capacity that was at least 55% of the normal predicted value, resulted in an increase in survival time, and accordingly reduced the risk of death of these individuals. However, there is no guidance or examples in the specification that shows that IPF can be prevented in any subject, including any individual who may be at risk for development of IPF. It is known in the art that IPF is a disease of unknown etiology, and little information is available regarding the course and natural history of IPF (see Condos *et al*, US 6,964,761, column 1, lines 25-26; see also Aggarwal *et al*, *Expert Opinion on Pharmacotherapy*, 2000, Vol. 1, p. 1423-1427, especially p. 1423). Because the underlying causes of IPF are unknown, a person of ordinary skill in the art would not

be able to predict which individuals are at risk of developing IPF, and thus would not be able to practice any method of preventing IPF. Furthermore, although the specification shows that IFN-γ administration increases survival time and reduces the risk of death of individuals having IPF, there is no guidance or examples showing that IFN-γ administration arrests the development of disease or reduces the rate of disease progression, or causes actual regression of the disease. Given the broadest reasonable interpretation, arresting the development of a disease or reducing the rate of disease progression, or regression of a disease could comprise inhibition or elimination of the underlying causes of disease, or a reduction in the symptoms of the disease. Although the specification shows an increase in survival of IPF patients after IFN-γ administration, the specification does not show that any symptoms of disease were reduced, or that disease development has been halted or regressed. As noted above, the art teaches unpredictability regarding the underlying causes of IPF, and therefore a person of ordinary skill in the art would not predict that the claimed method would inhibit disease development or cause regression of the disease.

Therefore, due to the excessive breadth of the claims in that Applicants have defined "treating" to mean preventing IPF, or inhibiting disease progression or causing regression of disease, the lack of guidance or examples showing that IPF can be prevented in patients "at risk" of developing IPF or of inhibiting disease progression or affecting disease regression, and the unpredictability inherent in the art regarding the underlying causes of IPF, a person of ordinary skill in the art would require further, undue experimentation in order to practice the claimed method in a manner commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 1-6, 8-14, 16-22, 24-30, and 32-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Ziesche *et al* ("Ziesche" - *New Eng. J. Med.*, 1999, Vol. 341, p. 1264-1269).

The claims of the instant invention are drawn to methods of treating IPF in an individual, increasing probability of survival of an individual having IPF, or reducing the risk of death of an individual having IPF, wherein said methods comprise administration of an effective amount of IFN-γ, and wherein said individual has a forced vital capacity that is at least about 55% of the normal predicted value. The claims further recite administration of about 200 μg IFN-γ, wherein the IFN-γ is administered three times weekly, administered subcutaneously, and administered with a corticosteroid. The claims also recite increasing the probability of survival of an individual by various percentages, or wherein the risk of death is two-fold or four-fold less than an expected risk of death with out IFN-γ.

Ziesche teaches a method treating humans having IPF by administration of IFN-γ. Specifically, Ziesche discloses treatment of IPF patients by administering IFN-γ and the corticosteroid prednisolone, wherein the IFN-γ was administered subcutaneously three times per week at a dose of 200 μg (see p. 1264, 1st column, 2nd paragraph). Ziesche also teaches that the patients who received IFN-γ had a forced vital capacity of 68 +/- 11 (% of predicted) (see Table 1). Ziesche also teaches that administration of IFN-γ improved total lung capacity of IPF patients (see p. 1265, 2nd column - p. 1267, 1st column), and therefore Ziesche teaches a method of treating IPF in a patient with a forced vital capacity of at least about 55% the normal predicted value, wherein said method comprises administration of an effective amount of IFN-γ. Although Ziesche does not explicitly teach an increase in the probability of survival or a reduction in the risk of death of the patients receiving IFN-γ, it would be expected that Ziesche's method would inherently increase the probability of survival of IPF patients by the recited percentages, and inherently reduce the risk of IPF patients. It would be expected, in absence of evidence to the contrary, that the method of Ziesche would inherently produce these effects because the method steps and patient populations of Ziesche are identical to those of the instant invention, and because Ziesche teaches that administration of IFN-γ to IPF patients resulted in an increase in pulmonary function compared to patients which did not receive IFN-γ. Because the USPTO does not have the facilities for testing the method of Ziesche, the burden is on the Applicants to show a novel and unobvious difference between the claimed methods and those of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). Furthermore, it is noted that because the method steps of Ziesche would inherently lead to an increased probability of survival or a reduction in the risk of death in a patient, the method of Ziesche is not patentably distinct from the presently claimed invention (Ex parte Novitski, 26 USPQ 1391).

2. Claims 1-6, 9, 11-14, 17, 19-22, 25, 27-30, and 33-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Condos *et al* ("Condos" - US 6,964,761).

The subject matter of the claims of the instant application is discussed above. Condos teaches a method of treating IPF by administration of IFN-γ. Specifically, Condos teaches administration of IFN-γ to patients suffering from IPF (column 1, lines 17-21) to patients with a forced vital capacity of 50% - 90% of predicted baseline (column 6, lines 37-38), and teaches administration 3 time weekly (column 2, lines 1-5), and further administration of a corticosteroid (claims 9-10). Although Condos does not explicitly teach an increase in the probability of survival or a reduction in the risk of death of the patients receiving IFN-γ, it would be expected that the method of Condos would inherently increase the probability of survival of IPF patients by the recited percentages, and inherently reduce the risk of IPF patients. It would be expected, in absence of evidence to the contrary, that the method of Condos would inherently produce these effects because the method steps and patient populations of Condos are identical to those of the instant invention. Because the USPTO does not have the facilities for testing the method of Condos, the burden is on the Applicants to show a novel and unobvious difference between the claimed methods and those of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7, 15, 23, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ziesche *et al* ("Ziesche" - *New Eng. J. Med.*, 1999, Vol. 341, p. 1264-1269).

The subject matter of the instant application and the teachings of Ziesche are discussed above. Claims 7, 15, 23, and 31 are drawn to methods of treating IPF by administration of IFN-γ in a dose of about 80 $\mu g/m^2$ to about 90 $\mu g/m^2$. As discussed above, Ziesche teaches treatment of IPF by administration of IFN-g, but is silent regarding administration of IFN-g in a dose of about 80 $\mu g/m^2$ to about 90 $\mu g/m^2$.

However, a person of ordinary skill in the art would have both the motivation and the ability to optimize the dosage of IFN-γ in order to practice the most effective method of treatment. MPEP 2144.05 states:

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 454, 105 USPQ 223, 235, (CCPA 1955).

In the instant case, the general conditions of the claims, namely treatment of IPF by administration of IFN-γ, is disclosed by Ziesche, and therefore it would be obvious to optimize the dosage of IFN-γ.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-35 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-35 of copending Application No. 11/487,733. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. In the instant case, claims 1-35 of the instant application are identical to claims 1-35 of the '733 application.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571)272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bruce D. Hissong
Art Unit 1646

/Robert Landsman/
Primary Examiner, Art Unit 1647